15/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09612997 98054343 PMID: 9391135
Respiratory syncytial virus (RSV) SH **and G proteins are not essential for viral replication in vitro: clinical evaluation and molecular characterization of a cold-passaged, attenuated** RSV **subgroup B mutant.**
Karron RA; Buonagurio DA; Georgiu AF; Whitehead SS; Adamus JE; Clements-Mann ML; Harris DO; Randolph VB; Udem SA; Murphy BR; Sidhu MS
Center for Immunization Research, Department of International Health, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD 21205, USA. rkarron@jhsph.edu
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Dec 9 1997, 94 (25) p13961-6, ISSN 0027-8424
Journal Code: PV3
Contract/Grant No.: AI-15095, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A live, cold-passaged (cp) candidate vaccine virus, designated **respiratory syncytial virus** (**RSV**) B1 cp-52/2B5 (cp-52), replicated efficiently in Vero cells, but was found to be overattenuated for **RSV** -seronegative infants and children. Sequence analysis of reverse-transcription-PCR-amplified fragments of this mutant revealed a large **deletion** spanning most of the coding sequences for the small hydrophobic (**SH**) and attachment (G) proteins. Northern blot analysis of cp-52 detected multiple unique read-through mRNAs containing **SH** and G sequences, consistent with a **deletion mutation** spanning the **SH** :G gene junction. Immunological studies confirmed that an intact G glycoprotein was not produced by the cp-52 virus. Nonetheless, cp-52 was infectious and replicated to high titer in tissue culture despite the absence of the viral surface **SH** and G glycoproteins. Thus, our characterization of this negative-strand RNA virus identified a novel replication-competent **deletion** mutant lacking two of its three surface glycoproteins. The requirement of **SH** and G for efficient replication in vivo suggests that selective **deletion** of one or both of these **RSV** genes may provide an alternative or additive strategy for developing an optimally attenuated vaccine candidate.

15/3,AB/8 (Item 2 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00511883
PRODUCTION OF INFECTIOUS RESPIRATORY SYNCYTIAL VIRUS **FROM CLONED NUCLEOTIDE SEQUENCES**
PRODUCTION DE VIRUS SYNCYTIAL RESPIRATOIRE INFECTIEUX A PARTIR DE SEQUENCES DE NUCLEOTIDES CLONES
Patent Applicant/Assignee:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by THE
COLLINS Peter L
Inventor(s):
COLLINS Peter L
Patent and Priority Information (Country, Number, Date):
Patent: WO 9712032 A1 19970403
Application: WO 96US15524 19960927 (PCT/WO US9615524)
Priority Application: US 957083 19950927
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO

NZ PL PT RO RU SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM
AZ BY KG KZ MD TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF
BJ CF CG CI CM ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 16569

English Abstract
Isolated polynucleotide molecules provide **RSV** genome and antigenomes, including that of human, bovine or murine **RSV** or **RSV** -like viruses, and chimera thereof. The recombinant genome or antigenome can be expressed with a nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large (L) polymerase protein, and an RNA polymerase elongation factor to produce isolated infections **RSV** particles. The recombinant **RSV** genome and antigenome can be modified to produce desired phenotypic changes, such as attenuated viruses for vaccine use.

Japanese Abstract
Cette invention concerne des molecules de polynucleotides isolees permettant d'obtenir des genomes et antigenomes de VSR, y compris ceux de VSR humains, bovins et murins ou de virus de type VSR, ainsi que leurs chimeres. Le genome ou antigenome recombine peut etre exprime a l'aide d'une proteine a nucleocapside (N), d'une phosphoproteine a nucleocapside (P), d'une proteine de polymerase de grande taille (L) et d'un facteur d'allongement d'ARN polymerase afin de produire des particules de VSR infectieuses isolees. Les genome et antigenome de VSR recombines peuvent etre modifies afin de produire les changements phenotypiques voulus, tel que des virus affaiblis pouvant etre utilises dans des vaccins.
?

18/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09646998 98105793 PMID: 9445048
The NS1 protein of human respiratory syncytial virus is a potent inhibitor of minigenome transcription and RNA replication.
Atreya PL; Peeples ME; Collins PL
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-0720, USA.
Journal of virology (UNITED STATES) Feb 1998, 72 (2) p1452-61, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The **NS1** protein (139 amino acids) is one of the two nonstructural proteins of human respiratory syncytial virus (RSV) and is encoded by a very abundant mRNA transcribed from the promoter-proximal RSV gene. The function of **NS1** was unknown and was investigated here by using a reconstituted transcription and RNA replication system that involves a minireplicon and viral proteins (N, P, L and M2-1) expressed from separate cotransfected plasmids. Coexpression of the **NS1** cDNA strongly inhibited transcription and RNA replication mediated by the RSV polymerase, even when the level of expressed **NS1** protein was substantially below that observed in RSV-infected cells. The effect depended on synthesis of **NS1** protein rather than **NS1** RNA alone. Transcription and both steps of RNA replication, namely, synthesis of the antigenome and the genome, appeared to be equally sensitive to inhibition. The efficiency of encapsidation of the plasmid-derived minigenome was not altered by coexpression of **NS1** , indicating that the inhibition occurs at a later step. In two different dicistronic minigenomes, transcription of each gene was equally sensitive to inhibition by **NS1** . This suggested that the gradient of transcriptional polarity was unaffected and that the effect of **NS1** instead probably involves an early event such as polymerase entry on the genome. **NS1** -mediated inhibition of transcription and RNA replication was not affected by coexpression of the M2 mRNA, which has two open reading frames encoding the transcriptional elongation factor M2-1 and the putative negative regulatory factor M2-2. The potent nature of the **NS1** -mediated inhibition suggests that negative regulation is an authentic function of the **NS1** protein, albeit not necessarily the only one.

18/3,AB/3 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128151668 CA: 128(13)151668m PATENT
Attenuated respiratory syncytial virus with a temperature-sensitive mutation in the polymerase and their use in vaccines
INVENTOR(AUTHOR): Murphy, Brian R.; Collins, Peter L.; Whitehead, Stephen S.; Bukreyev, Alexander A.; Juhasz, Katalin; Teng, Michael N.
LOCATION: USA
ASSIGNEE: United States Dept. of Health and Human Services; Murphy, Brian R.; Collins, Peter L.; Whitehead, Stephen S.; Bukreyev, Alexander A.; Juhasz, Katalin; Teng, Michael N.
PATENT: PCT International ; WO 9802530 A1 DATE: 19980122
APPLICATION: WO 97US12269 (19970715) *US 21773 (19960715) *US 46141 (19970509) *US 47634 (19970523)
PAGES: 242 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-007/04A;

C12N-007/01B; A61K-039/155B; C12N-015/45B; C12N-007/00B
DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; KE; LS; MW; SD; SZ; UG ; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

18/3,AB/5 (Item 2 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00511883
PRODUCTION OF INFECTIOUS RESPIRATORY SYNCYTIAL VIRUS **FROM CLONED NUCLEOTIDE SEQUENCES**
PRODUCTION DE VIRUS SYNCYTIAL RESPIRATOIRE INFECTIEUX A PARTIR DE SEQUENCES DE NUCLEOTIDES CLONES
Patent Applicant/Assignee:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by THE
COLLINS Peter L
Inventor(s):
COLLINS Peter L
Patent and Priority Information (Country, Number, Date):
Patent: WO 9712032 A1 19970403
Application: WO 96US15524 19960927 (PCT/WO US9615524)
Priority Application: US 957083 19950927
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 16569

English Abstract
Isolated polynucleotide molecules provide RSV genome and antigenomes, including that of human, bovine or murine RSV or RSV-like viruses, and chimera thereof. The recombinant genome or antigenome can be expressed with a nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large (L) polymerase protein, and an RNA polymerase elongation factor to produce isolated infections RSV particles. The recombinant RSV genome and antigenome can be modified to produce desired phenotypic changes, such as attenuated viruses for vaccine use.

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?

21/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09345701 97332323 PMID: 9188557
Analysis of the gene start and gene end signals of human respiratory syncytial virus : **quasi-templated initiation at position 1 of the encoded mRNA.**
Kuo L; Fearns R; Collins PL
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892-0720, USA.
Journal of virology (UNITED STATES) Jul 1997, 71 (7) p4944-53, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The gene start (GS) and gene end (GE) transcription signals of human respiratory syncytial virus (RSV) strain A2 were analyzed in helper-dependent monocistronic and dicistronic minireplicons which were complemented by a standard RSV strain. The GS signal, which is the start site for mRNA synthesis, is highly conserved for the first nine genes: 3'-CCCCGUUUA(U/C) (negative sense). This conserved version of the signal was analyzed by "saturation" mutagenesis, in which all 10 positions, as well as one downstream and one upstream position, were changed one at a time into each of the other three nucleotides. Most of the positions appear to contribute to the signal: positions 1, 3, 6, 7, and, in particular, 9 were the most sensitive, whereas position 5 was relatively insensitive. The effect of nucleotide substitution in the first position of the signal was examined further by cDNA cloning and sequence analysis of the residual mRNA which was produced. For the two mutants examined (1C to U, and 1C to A), the site of initiation was unchanged. However, the mRNAs were dimorphic with regard to the assignment of the 5'-terminal nucleotide: two-thirds contained the predicted mutant substitution, and one-third contained the parental assignment. Intracellular minigenome contained only the mutant assignment, indicating that the heterogeneity was at the level of transcription by the RSV polymerase. This suggests that the templated mutant assignment at position 1 can sometimes be overridden by an innate preference for the parental assignment, a phenomenon which we dubbed quasi-templated initiation. The GS signal of the L gene, encoding the 10th RSV mRNA, contains three differences (3'-CCCUGUUUUA) compared to the conserved version. It was shown to be equal in efficiency to the conserved version. This was unexpected, since the saturation mutagenesis described above indicated that U in place of A at position 9 should be highly inhibitory. Instead, the A at position 10 of the L GS signal was found to be critical for activity, indicating that an essential A residue indeed was present in both versions of the GS signal but that its spacing differed. The GE signal, which directs termination and polyadenylation, has more sequence diversity in nature than does the GS signal. The naturally occurring GE signals of strain A2 were compared by their individual incorporation into a dicistronic minigenome. They were similar in the ability to produce translatable mRNA except in the cases of NS1 and **NS2** , which were approximately 60% as efficient.

21/3,AB/2 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128151668 CA: 128(13)151668m PATENT
Attenuated respiratory syncytial virus with a temperature-sensitive mutation in the polymerase and their use in vaccines

INVENTOR(AUTHOR): Murphy, Brian R.; Collins, Peter L.; Whitehead, Stephen S.; Bukreyev, Alexander A.; Juhasz, Katalin; Teng, Michael N.
LOCATION: USA
ASSIGNEE: United States Dept. of Health and Human Services; Murphy, Brian R.; Collins, Peter L.; Whitehead, Stephen S.; Bukreyev, Alexander A.; Juhasz, Katalin; Teng, Michael N.
PATENT: PCT International ; WO 9802530 A1 DATE: 19980122
APPLICATION: WO 97US12269 (19970715) *US 21773 (19960715) *US 46141 (19970509) *US 47634 (19970523)
PAGES: 242 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-007/04A; C12N-007/01B; A61K-039/155B; C12N-015/45B; C12N-007/00B
DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; KE; LS; MW; SD; SZ; UG ; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

21/3,AB/5 (Item 1 from file: 654)
DIALOG(R)File 654:US PAT.FULL.

02719054
Utility
RESPIRATORY SYNCYTIAL VIRUS RIBOZYMES
[Enzymatic RNA molecule which specifically cleaves genomoc RNA of respiratory syncytial virus or messenger RNA encoded by said virus in specified region]

PATENT NO.: 5,693,532
ISSUED: December 02, 1997 (19971202)
INVENTOR(s): McSwiggen, James, Boulder, CO (Colorado), US (United States of America)
Draper, Kenneth, Boulder, CO (Colorado), US (United States of America)
Pavco, Pam, Layfayette, CO (Colorado), US (United States of America)
Woolf, Tod, Watertown, MA (Massachusettes), US (United States of America)
ASSIGNEE(s): Ribozyme Pharmaceuticals, Inc , (A U.S. Company or Corporation), Boulder, CO (Colorado), US (United States of America)
[Assignee Code(s): 38218]
EXTRA INFO: Assignment transaction [Reassigned], recorded July 16, 1999 (19990716)
APPL. NO.: 8-334,847
FILED: November 04, 1994 (19941104)

FULL TEXT: 9842 lines

ABSTRACT

An enzymatic RNA molecule which cleaves respiratory syncytial virus (RSV) genomic and RSV encoded RNA.
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